

## REMARKS

### I. Status of the Claims

Claims 1-101 were filed with the application. Claims 1-58, 60, 63-69 and 71-101 have been canceled. Thus, claims 59, 61, 62 and 70 are under consideration and have been examined. Claim 59 is hereby amended. Thus, claims 59 (amended), 61, 62 and 70 are presented for reconsideration. Support for the amendment to claim 59 can be found in the specification at page 2, line 1; page 14, lines 13-15; and pages 90-91.

All claims are rejected under 35 U.S.C. §112, second paragraph. All claims also stand rejected under 35 U.S.C. §102 and 35 U.S.C. §103. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

### II. Rejections Under 35 U.S.C. §112, Second Paragraph

The examiner has again rejected claims 59, 61, 62 and 70 under the second paragraph of §112 as being indefinite for failing to particularly point out and distinctly claim the subject matter. The examiner has merely repeated his prior §112 objections to the language in the claims, without addressing the arguments made in any prior response or the filed Appeal Brief. Applicants contend the argument presented in the Appeal Brief on record should be sufficient to overcome all §112 objections to the claims as written and as now amended. That argument, restated here for clarity, is that the very essence of the present claims is to identify molecules that may modify MCIP expression *in either direction – up or down*; hence the use of the word *modulation*, which is generic to up- or down-regulation, accurately reflects the intent of the claim, and is thus very much correct in its usage. By way of example, the Merriam-Webster dictionary defines modulate as to “vary” or “adjust” or “alter” and does not describe a direction

in which such variation or adjustment occurs. A modulator is thus, by definition, something that is capable of varying something else, and a modulator of MCIP expression can therefore vary the expression of MCIP in any direction, up or down. There is nothing indefinite about this recitation, and reversal of this rejection is respectfully requested.

In the most recent Office Action, the examiner objects to claims 61 and 62 by arguing that a modulator cannot be both an agonist and an antagonist, and hence these recitations in claims 61 and 62, respectfully, are also unclear. Nothing could be further from the truth. Claims 61 and 62 are dependent claims. Thus, they further limit the subject matter of claim 59, which as already pointed out, is generic with respect to the direction of regulation. There is absolutely nothing indefinite about these claims, and in point of fact these claims address the issue raised by the examiner's faulty rejection of the word modulator by giving a specific direction to the modulation that must occur. Reversal of this rejection is respectfully requested as well.

Claim 70 is also rejected over the term "second pharmaceutical agent." Applicants previously amended claim 70 to clarify that the second pharmaceutical agent is distinct from the agent provided in claim 59. Applicants have previously attempted to amend claim 59 to specify a first pharmaceutical agent (*i.e.*, the modulator), in that claim, but entry of this amendment was denied. Applicants are more than willing to provide an additional amendment, or authorize the examiner to make such an amendment. Even if this amendment is not entered, however, appellants submit that one of skill in the art would recognize that the "second pharmaceutical agent" of claim 70 is in addition to the modulator of claim 59, and thus there is no issue of indefiniteness. Reversal of this rejection is respectfully requested.

The examiner also objects to the term "small molecule modulator" as being undefined in the specification. That assertion is erroneous. The specification defines and describes a wide

variety of agents that could be classified as small molecules, and one of skill in the art would not need an exhaustive recitation or a glossary listing to define what a small molecule refers to given the extensive teachings of the specification. Reversal of these rejections is respectfully requested.

### III. Rejections Under 35 U.S.C. §102

Claims 59, 61, 62 and 70 are rejected under 35 U.S.C. §102(b) as being anticipated by Medina *et al.* For literal anticipation of a claim, “a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter.” *PPG Industries Inc. v. Guardian Industries Corp.*, 37 USPQ.2d 1618, 1624 (Fed. Cir. 1996). Applicants contend that the examiner has misread the reference and that fact, coupled with the current amendment to Claim 59, removes this reference as an anticipation. The claim as written is drawn specifically to modulating muscle cell growth, including the step of “identifying” a patient in need of muscle cell modulation. Medina *et al.*, is an *in vitro* experimental application of cyclosporin to smooth muscle cells. No patients to be treated are identified in this paper, and the fact that a reference discloses application of a putative modulator of MCIP to cells does not disclose the stated element of identifying a human patient. Additionally, the reference specifically targets smooth muscle cells, and as amended, all of the claims now refer to modulation of striated muscle cells, a feature which is not disclosed by this reference. In point of fact, smooth muscle cells are **not** striated muscle cells, and thus the claims cannot be anticipated by this reference, as nowhere in this reference are striated muscle cells exposed to a modulator of MCIP. In light of these statements and the amendments presented herein, reconsideration and reversal of this rejection is respectfully requested.

#### IV. Rejections Under 35 U.S.C. §103

Claims 59, 61, 62 and 70 are rejected under 35 U.S.C. §103(a) as allegedly being obvious in light of Chin *et al.*, Sussman *et al.*, and Fuentes *et al.* Applicants remind the examiner that they have previously submitted an Inventors' Declaration under 37 C.F.R. §1.131 to swear behind the Fuentes *et al.* reference, and that the examiner has now twice cited this reference against Applicants AFTER the declaration was received. Thus, the rejection over Fuentes *et al.* will not be further addressed.

As for the rejections stemming from Chin *et al.*, and Sussman *et al.*, the examiner is improperly relying on inherency in the context of an obviousness rejection. Rather, the proper analysis should focus on whether these references would render the invention obvious based on the knowledge that one of skill in the art would gain from the references, not based on what is later discovered to be true. The fact that a specific result or pathway might flow inherently from the practice of a process or discovery of a partial biological pathway is immaterial if the skilled artisan "would not appreciate or recognize that inherent result." *In re Naylor*, 152 USPQ 106 (CCPA 1966). Furthermore, *In re Spormann*, 150 USPQ 449 (CCPA 1966) says that "the inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." Both of the cited references existed before the knowledge of MCIP's role in cardiac biology was fully elucidated. The fact that calcineurin was eventually shown to modulate MCIP does not make it obvious to one of skill in the art at the time of these references that modulating MCIP could be accomplished by modulating calcineurin.

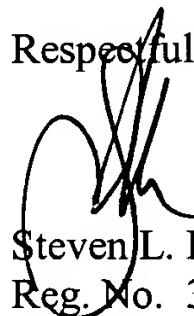
More to the point, neither reference renders obvious the steps of (i) selecting a human patient or (ii) selecting a modulator of MCIP with which to treat that human patient, both of

which are affirmative recitations in the instant claims, for the simple reason that *neither step is taught or suggested by the references*. Thus, the examiner has simply ignore required elements of the claims, relying instead on inherency to support either an obviousness rejection. As stated above, this not proper. In light of these statements, reconsideration and reversal of these rejections is respectfully requested.

#### IV. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to this effect is earnestly solicited. Should Examiner Liu have any questions regarding this response, he is invited to contact the undersigned attorney at (512) 536-3184 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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